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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,994	BAUMANN ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-21 and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted April 6, 2004 wherein claims 11, 13, 15-18, and 20 are amended and new claims 30-34 are introduced. This application was filed July 28, 2003.

Claims 1-34 are pending in this application.

Claims 11-21 and 27-34 as amended are examined on the merits herein.

Applicant's amendment, submitted April 6, 2007, with respect to the rejection of instant claims 11, 12, 14, and 19-21 under 35 USC 112, second paragraph, for being indefinite for reciting the phrase, "biologically active derivative thereof," has been fully considered and found to be persuasive to remove the rejection as the claims as amended recite a specific range of structures considered to be biologically active derivatives of the claimed compound. Therefore the rejection is withdrawn.

Applicant's declaration of Neil A. Swanson, submitted April 17, 2007, under 37 CFR 1.132, is acknowledged and will be further discussed below.

Applicant's amendment, submitted April 6, 2007, with respect to the rejection of instant claims 11, 13, 14, and 19 under 35 USC 102(b) for being anticipated by Stockfleth et al., has been fully considered and found to be persuasive to remove the rejection for these claims only as the claims as amended are drawn only to treating fine lines and clinical wrinkles, and not to a method of treating actinic keratosis. Therefore

the rejection is withdrawn. Note that the rejection of claims 20, 21, 27, and 28 for being anticipated by Stockfleth et al. is not withdrawn in response to this amendment as these claims still encompass a method of treating actinic keratosis, as described below.

Applicant's amendment, submitted April 6, 2007, with respect to the rejection of instant claims 12 and 15-18 under 35 USC 103(a) for being obvious over Stockfleth et al., has been fully considered and found to be persuasive to remove the rejection for these claims only as the claims as amended are drawn only to treating fine lines and clinical wrinkles, and not to a method of treating actinic keratosis. Therefore the rejection is withdrawn. Note that the rejection of claim 29 for being obvious over Stockfleth et al. is not withdrawn in response to this amendment as this claim still encompasses a method of treating actinic keratosis, as described below.

Applicant's amendment, submitted April 6, 2007, with respect to the rejection of instant claims 11-19 under 35 USC 103(a) for being obvious over Maibach et al., has been fully considered and found to be persuasive to remove the rejection for these claims only as the claims as amended are drawn only to treating fine lines and clinical wrinkles, and not to a method of treating hyperpigmentation. Therefore the rejection is withdrawn. Note that the rejection of claims 20 and 21 for being obvious over Maibach et al. is not withdrawn in response to this amendment as this claim still encompasses any method in which imiquimod is applied to the skin, as described below.

Applicant's amendment, submitted April 6, 2007, necessitates the following new grounds of rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the specification fails to enable one skilled in the art to treat the recited disorders using **the specific compounds recited in claims 33 and 34**.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method comprising administering a dermatological composition to a subject having fine lines and/or wrinkles.

The state of the prior art: Imiquimod, a toll-like receptor agonist and interferon inducer, is known to be useful as a dermatological agent for treating a variety of conditions such as precancerous lesions and viral infection. Miller et al. (US patent publication 2004/0180919, application 10/799999, cited in PTO-892) additionally discloses that imiquimod is useful for treating fine lines and wrinkles.

The specific compounds disclosed in instant claims 33 and 34 share the core imizadoquinolone structure with imiquimod, but they differ in that the compounds of claim 33 possess a piperidyl-alkyl-substituent at the 1-N position, while those of claim 34 leave this nitrogen entirely unsubstituted. These compounds are never disclosed to possess toll-like receptor activity, interferon induction, or any cytotoxic, antiviral, or antitumor activity. Rather, the compounds of claim 33 are disclosed by Izumi et al. (Reference included with PTO-1449) to not be IFN inducers and in fact to suppress TNF-α, (abstract, p. 2544, left column, first paragraph, p. 2545, left column, first paragraph) and the compounds of claim 34 are disclosed by van Galen et al. (Reference included with PTO-1449) to be adenosine receptor agonists, with no mention of toll-like receptor activation or interferon induction. Based on these references, it is seen to be unlikely that these compounds will act on the same target, work by the same mechanism, or produce the same effect as imiquimod or any of the other claimed toll-like receptors. Therefore the prior art does not provide any reason to expect that these compounds possess the claimed activity.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: According to Silverman (Reference included with PTO-892) Agonists against a particular receptor exhibit close structural similarity, while there are a wider range of structures that act as antagonists. (p. 69, first paragraph) It is easier to design an antagonist than an agonist. (p. 70, first paragraph) Silverman also discloses that most xenobiotic compounds that interact with receptors are antagonists. (p. 70, third paragraph) Thus the design and/or identification of new agonists at a particular receptor is highly unpredictable, and a randomly chosen derivative of a particular agonist is likely to be an antagonist..

The Breadth of the claims: The claimed invention includes a method for treating certain dermatological conditions by administering a certain class of compounds.

The amount of direction or guidance presented: Applicant's disclosure does not contain any information about the biological properties, molecular targets, or therapeutic utility of these compounds aside from the statement on p. 11 that derivatives of imiquimod described in the Izumi et al. and van Galen et al. references can be used in the claimed invention. No evidence is provided that these compounds are actually toll-like receptor activators or interferon inducers.

The presence or absence of working examples: The only working examples provided concern the dermatological use of imiquimod, rather than any of the compounds of claims 33 and 34.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the identification of novel receptor agonists. See MPEP 2164.

The quantity of experimentation necessary: In order to make and use the invention of claims 33 and 34, one skilled in the art would have to determine the biological activity and mode of action of the claimed compounds. Applicant has provided no evidence that these compounds are toll-like receptor agonists, or that they are capable of producing the same biological effects as imiquimod. The only evidence provided is their alleged structural similarity to imiquimod. As discussed earlier, it is much easier to antagonize than to activate a receptor, and many compound that bear some structural similarity to known agonists are actually antagonists.

In the absence of any actual evidence that the compounds of claims 33 and 34 are useful in the claimed methods, one skilled in the art would have to perform all of the experimentation involved in determining the activity of these compounds and developing a method of using them to treat wrinkles and fine lines. Undertaking this process of experimentation, with no assistance from the prior art or Applicant's disclosure, and no expectation of success, constitutes an undue and unpredictable experimental burden in order to practice the claimed invention.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the state of the art and the lack of guidance and working examples, Applicants fail to

provide information sufficient to practice the claimed invention. Because applicant's amendment necessitated this new ground of rejection, the rejection is made **FINAL**.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11-17, 19-21, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Miller et al. (US patent publication 2004/0180919, application 10/799999, cited in PTO-892) Miller et al. discloses a method of improving skin quality by topical administration of an immune response modifier. (p. 1, paragraphs 0004-0005 and 0015) In particular, improving skin quality involves treating fine lines and wrinkles. (p. 1, paragraphs 0001 and 0007, p. 4, paragraph 42) Suitable immune response modifiers include imidazoquinoline amines, (p. 2, paragraph 0024) in particular 1-(2-methylpropyl)-1H-imidazo[4,5-c]quinolin-4-amine, otherwise known as imiquimod. (p. 3, paragraph 0025) The active agent is administered in a formulation having any one of various concentrations including about 1% or 5%. (p. 4, paragraph 0038) The composition is administered 2, 3, 5, or 7 times a week. (p. 4, paragraphs 0047 and 0048, p. 5, paragraph 0060 and table 1) In one specific example, 5% imiquimod is

administered daily to treat wrinkles, and the subjects are evaluated by visual and photographic assessment. (p. 6, paragraphs 0067-0074) The various embodiments disclosed in this reference are the same as the method of treating clinical wrinkles recited in the instant claims. Furthermore they are reasonably considered to be a method of inducing an immune cytotoxic response in a section of damaged dermal or epidermal tissue, because they comprise administering the same compound to the same subjects as instant claims 20 and 21. Although Miller et al. does not explicitly state that the applied composition attracts macrophage cells to the area, activates the toll-like receptor 7, or identifies a precancerous region of skin, all of these elements are inherent in the method as disclosed by Miller et al. The mechanism by which the claimed method works is not given patentable weight over the prior art. The steps disclosed in the reference are the same as in the instant claims, administering the same compound in the same amounts to the same or similar cells or subjects by the same mode of administration. See *Ex parte Novitski* 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that the claiming of a new use, new function, or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3c. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it relates to the claimed invention herein. Thus Miller et al. anticipates the claimed invention. Because applicant's amendment necessitated this new ground of rejection, the rejection is made **FINAL**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (US patent publication 2004/0180919, application 10/799999, cited in PTO-892) The disclosure of Miller et al is discussed above. Miller et al. does not specifically disclose a method comprising administration of imiquimod in a composition comprising 1.25% imiquimod.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Miller et al. administering the imiquimod in a concentration of 1.25%. One of ordinary skill in the art would have been motivated to modify the invention in this way because Miller et al. already discloses various concentrations encompassing 1.25%, including about 1%. One of ordinary skill in the art would reasonably have expected success because adjusting the dosage level of a known compound is well within the ordinary level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because applicant's amendment necessitated this new ground of rejection, the rejection is made **FINAL**.

Claims 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (US patent publication 2004/0180919, application 10/799999, cited in

PTO-892) in view of Gerster (US patent 4689338, cited in PTO-1449) The disclosure of Miller et al is discussed above. Miller et al. does not specifically disclose a method comprising administering one of the imiquimod derivatives disclosed in instant claims 30 and 32.

Gerster discloses a class of compounds including various compounds of instant claims 30 and 32. (column 2, line 1 – column 3, line 25, R_1 = benzyl, phenylethyl, or phenyl, substituted with 1-2 C_{1-4} alkyl groups, R_2 = H, n = 0) These compounds exhibit antiviral activity, (column 6, lines 45-68) and are immunomodulators and interferon inducers. (column 8, lines 12-20), also table XIII in column 33)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention if Miller et al. with the aforementioned compounds of Gerster. One of ordinary skill in the art at the time of the invention would have been motivated to use these compounds because these compounds are disclosed to be immunomodulators and interferon inducers, and thus reasonably considered to be immune response modifiers according to Miller et al. Also, the compounds are structurally similar to imiquimod and other imiadazoquinolines disclosed by Miller et al. One of ordinary skill in the art would have reasonably expected success because substituting one active agent with another having the same activity is within the ordinary and routine level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious. Because applicant's amendment necessitated this new ground of rejection, the rejection is made **FINAL**.

The following grounds of rejection of record in the previous office action are maintained:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 21, 27, and 28, are rejected under 35 U.S.C. 102(b) as being anticipated by Stockfleth et al. (Reference included with PTO-892) Stockfleth et al. discloses a method of treating actinic keratosis, a non-malignant, precancerous lesion of the skin caused by aging or excessive UV exposure. (p. 1050, left column, first paragraph) The method comprises administering a 5% imiquimod (1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine) cream 2-3 times a week to the affected area, and successfully removed the lesions without recurrence. (p. 1051, right column, last paragraph – p. 1052, left column, second paragraph) This treatment regimen is identical to that disclosed in instant claims 20 and 21. During treatment, the AK lesions became inflamed (erythema) and were clearly visible by visual assessment. (p. 1052, left column, third paragraph, p. 1051, figure 1, particularly frames B and C) Stockfleth et al. also discloses that this inflammatory response may be used as a clinical marker to indicate the initiation of an immune response. Although Stockfleth et al. does not explicitly state that the applied composition attracts macrophage cells to the area, activates the toll-like receptor 7, or identifies a precancerous region of skin, all of these

elements are inherent in the method as disclosed by Stockfleth et al. The steps disclosed in the reference are the same as in the instant claims, administering the same compound in the same amounts to the same or similar cells or subjects by the same mode of administration. See *Ex parte Novitski* 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that the claiming of a new use, new function, or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3c. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it relates to the claimed invention herein.

The claimed invention is thus anticipated by Stockfleth et al.

Response to Argument: Applicant's argument, submitted April 6, 2007 with respect to the above grounds of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the claims as amended no longer include within their scope a method of treating actinic keratosis according to Stockfleth et al. Further, the declaration under 37 CFR 1.132, by Neil A. Swanson, states that both actinic keratosis and warts differ significantly from non-cancerous intrinsically aged or photodamaged skin, and in particular that they do not fit within the scope of skin having "fine lines or wrinkles," in the language of the claims as amended. However, claims 20, 21, 27, and 28 were not amended with respect to the scope of conditions being treated. Claims 20 and 21 encompass any method whereby one of the claimed compounds is administered to a subject's skin. Claims 27 and 28 still explicitly

claim a method for identifying a precancerous region of skin. (e.g. an actinic keratosis) Therefore the rejection is maintained and made **FINAL**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stockfleth et al. (Reference included with PTO-892) Stockfleth et al. discloses a method of treating actinic keratosis, a non-malignant, precancerous lesion of the skin caused by aging or excessive UV exposure. (p. 1050, left column, first paragraph) The method comprises administering a 5% imiquimod (1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine) cream 2-3 times a week to the affected area, and successfully removed the lesions without recurrence. (p. 1051, right column, last paragraph – p. 1052, left column, second paragraph) This treatment regimen is identical to that disclosed in instant claims 11, 13, 14, and 19-21. During treatment, the AK lesions became inflamed (erythema) and were clearly visible by visual assessment. (p. 1052, left column, third paragraph, p. 1051, figure 1, particularly frames B and C) Stockfleth et al. also discloses that this inflammatory response may be used as a clinical marker to indicate the initiation of an immune response. Stockfleth et al. does not specifically disclose a method comprising

daily administration of imiquimod, or administration of imiquimod in a composition comprising 1-2% imiquimod.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Stockfleth et al. administering the imiquimod daily in a concentration of 1-2%. One of ordinary skill in the art would have been motivated to modify the invention in this way because the method as practiced by Stockfleth et al. leads to a significant inflammatory response which causes discomfort and inconvenience. Therefore a lower dose administered more frequently would be expected to lead to less severe irritation. One of ordinary skill in the art would reasonably have expected success because adjusting the dosage level and frequency of administration is well within the ordinary level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's argument, submitted April 6, 2007 with respect to the above grounds of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the claims as amended no longer include within their scope a method of treating actinic keratosis according to Stockfleth et al. Further, the declaration under 37 CFR 1.132, by Neil A. Swanson, states that both actinic keratosis and warts differ significantly from non-cancerous intrinsically aged or photodamaged skin, and in particular that they do not fit within the scope of skin having "fine lines or wrinkles," in the language of the claims as amended. However, claim 29 was not amended with respect to the scope of conditions being

treated, and still explicitly claims a method for identifying a precancerous region of skin. (e.g. an actinic keratosis) Therefore the rejection is maintained and made **FINAL**.

Claims 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maibach et al. (US patent application 10/178082, cited in PTO-892) Maibach et al. discloses a method for treating hyperpigmentation of the skin resulting from various causes including UV exposure or age (paragraph 0006, 0016, 0017) comprising administering an active agent selected from a number of compounds including proinflammatory agents such as imiquimod (1-isobutyl-1H-imidazo [4,5-C]quinolin-4-amine) in combination with various skin penetration enhancers. (paragraph 0092) The composition is preferably administered in one or more doses per day. (paragraph 0130) In two examples given of therapeutic methods, changes in skin appearance are measured by photographic assessment. Two examples of pharmaceutical formulations are given including 1% hydroquinone as the active agent. Maibach et al. does not specifically disclose methods involving a composition consisting essentially of imiquimod, or compositions consisting essentially of 1.25%, 1-2%, or 5% imiquimod.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Maibach et al. using imiquimod as the active ingredient. It would also have been obvious to one of ordinary skill in the art to use a composition consisting essentially of 1-2%, 1.25%, or 5% imiquimod, as described by instant claims 13 and 15-18. One of ordinary skill in the art would have been motivated to use imiquimod as the active ingredient because Maibach recites imiquimod as one

possible active ingredient for use in the invention. One of ordinary skill in the art would have been motivated to use a composition consisting essentially of 1-2%, 1.25%, or 5% imiquimod because the examples given by Maibach et al. consist essentially of 1% active agent, which is within the approximate range of these values. One of ordinary skill in the art would have reasonably expected success in using imiquimod because Maibach discloses that the invention will work with imiquimod, and would have reasonably expected success in using a composition consisting essentially of 1-2%, 1.25%, or 5% imiquimod because determining the precise amounts of active ingredient to apply is well within the ordinary level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's argument, submitted April 6, 2007 with respect to the above grounds of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the claims as amended no longer include within their scope a method of treating actinic keratosis according to Stockfleth et al. Further, the declaration under 37 CFR 1.132, by Neil A. Swanson, states that both actinic keratosis and warts differ significantly from non-cancerous intrinsically aged or photodamaged skin, and in particular that they do not fit within the scope of skin having "fine lines or wrinkles," in the language of the claims as amended. However, claims 20 and 21 were not amended with respect to the scope of conditions being treated. Claims 20 and 21 encompass any method whereby one of the claimed compounds is administered to a subject's skin, including those wherein the composition

is applied to treat warts, hyperpigmentation, or any other condition that is not fine lines or wrinkles. Therefore the rejection is maintained and made **FINAL**.

Conclusion

No claims are allowed in this application. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson
Patent Examiner
AU 1623
5/11/07

Anna Jiang
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